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two markers, one associated with osteoblasts and targeted to evaluation of therapeutic effect, and the other associated with osteoclasts and targeted to evaluation of worsening of the disease.

B2
8. (Amended) A method of evaluating the therapeutic efficacy of a drug using a marker that reflects the activity of osteoblasts and a marker that reflects the action of osteoclasts, whereby the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed correctly by monitoring said two markers, one associated with osteoblasts and targeted to evaluation of therapeutic effect, and the other associated with osteoclasts and targeted to evaluation of worsening of the disease.

B3
3. (Amended) The method according to claim 1, wherein the marker that reflects the activity of osteoblasts is:

- B3*
(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or
(2) Bone specific alkaliphosphatase and osteocalcin.

B4
5. (Amended) The method according to claim 1, wherein the marker that reflects the action of osteoclasts is

B4
deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

B5
7. (Amended) The method according to claim 6, which is based on the value of a crossover index between osteocalcin and Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and the measured value of Carboxyterminal telopeptide of type I collagen, or on the value of a crossover index between osteocalcin and Bone specific alkaliphosphatase and the measured value of Carboxyterminal telopeptide of type I collagen.

B6
13. (Amended) The method according to claim 8, wherein the marker that reflects the activity of osteoblasts is:

- B6*
(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or
(2) Bone specific alkaliphosphatase and osteocalcin.

B7
15. (Amended) The method according to claim 8, wherein the marker that reflects the action of osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.

B8
17. (Amended) The method according to claim 16, which is based on the value of a crossover index between

osteocalcin and Carboxyterminal propeptide of type I pro-collagen or Amino terminal propeptide of type I procollagen and the measured value of Carboxyterminal telopeptide of type I collagen, or on the value of a crossover index between osteocalcin and Bone specific alkaliphosphatase and the measured value of Carboxyterminal telopeptide of type I collagen.

6. (Amended) The method according to claim 1, based on the value of a crossover index which is the ratio between a marker associated with the phase of calcification and a marker associated with the phase of osteoblast proliferation and matrix formation and the measured value of the marker that reflects the action of osteoclasts, or on the value of a crossover index which is the ratio between a marker associated with the phase of calcification and a marker associated with the phase of matrix maturation and the measured value of a marker associated with bone type I collagen.

16. (Amended) The method according to claim 8, based on the value of a crossover index which is the ratio between a marker associated with the phase of calcification and a marker associated with the phase of osteoblast proliferation and matrix formation and the measured value of the marker that reflects the action of osteoblasts, or on the